

# NASH-linked changes impact metformin pharmacokinetics

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(HealthDay)—Nonalcoholic steatohepatitis (NASH)-associated changes in liver function affect kidney transporter expression and metformin pharmacokinetics, according to an experimental study published online May 27 in *Diabetes Care*.

John D. Clarke, Ph.D., from the University of Arizona in Tucson, and colleagues examined how NASH affects kidney transporter expression and [metformin](#) pharmacokinetics. They administered a single oral dose of [<sup>14</sup>C] metformin to C57BL/6 (WT) mice and mice with diabetes (*ob/ob*). Mice were fed a methionine and choline deficient (MCD) diet or a control diet.

The researchers found that, compared with WT/Control mice, metformin plasma concentrations were slightly elevated in the WT/MCD and *ob*/Control groups, and 4.8-fold higher in *ob*/MCD mice. In both

genotypes, the MCD diet significantly increased plasma half-life and mean residence time, and decreased oral clearance. These changes were attributable to *ob/ob* and MCD diet-specific reductions in the kidney mRNA expression of Oct2 and Mate1; Oct1 mRNA expression was reduced only in *ob/MCD* [mice](#).

"These results indicate that the diabetic *ob/ob* genotype and the MCD disease model alter kidney transporter expression and alter the pharmacokinetics of metformin, potentially increasing the risk of drug toxicity," the authors write.

**More information:** [Abstract](#)  
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